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Invited review

Routine and quantitative EEG in mild traumatic brain injury

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Abstract

This article reviews the pathophysiology of mild traumatic brain injury, and the findings from EEG and quantitative EEG (QEEG) testing after such an injury.

Research on the clinical presentation and pathophysiology of mild traumatic brain injury is reviewed with an emphasis on details that may pertain to EEG or QEEG and their interpretation. Research reports on EEG and QEEG in mild traumatic brain injury are reviewed in this setting, and conclusions are drawn about general diagnostic results that can be determined using these tests. QEEG strengths and weaknesses are reviewed in the context of factors used to determine the clinical usefulness of proposed diagnostic tests.

Clinical signs, symptoms, and the pathophysiologic axonal injury and cytotoxicity tend to clear over weeks or months after a mild head injury. Loss of consciousness might be similar to a non-convulsive seizure and accompanied subsequently by postictal-like symptoms. EEG shows slowing of the posterior dominant rhythm and increased diffuse theta slowing, which may revert to normal within hours or may clear more slowly over many weeks. There are no clear EEG or QEEG features unique to mild traumatic brain injury. Late after head injury, the correspondence is poor between electrophysiologic findings and clinical symptoms. Complicating factors are reviewed for the proposed commercial uses of QEEG as a diagnostic test for brain injury after concussion or mild traumatic brain injury.

The pathophysiology, clinical symptoms and electrophysiological features tend to clear over time after mild traumatic brain injury. There are no proven pathognomonic signatures useful for identifying head injury as the cause of signs and symptoms, especially late after the injury.

Keywords: EEG; QEEG; Quantitative EEG; Head trauma; Brain injury; Concussion

1. Introduction

Mild traumatic brain injury (MTBI) is a medical problem commonly encountered today in the general community. Some patients complain of persistent cognitive difficulties after such an injury. Quantitative EEG (QEEG) has been proposed as a clinical diagnostic test to identify, confirm, measure and localize brain injury among those patients.

This report reviews the physiology of MTBI, as well as the literature on traditional EEG abnormalities among patients. QEEG reports are discussed in that context. Techniques reviewed here include both QEEG discriminant analysis and the numerical tables of frequency analysis with normative database comparison.

This report generally avoids covering severe head injury, except where needed to understand better the findings in minor head injury. Nor does this report cover evoked potentials, event-related potentials, or recordings during cognitive activation tasks.

2. Concussion and mild traumatic brain injury

2.1. Terminology

Several terms are in common use to describe MTBI. The term *concussion* is an older terminology that still is often

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used in discussions with the public. Mild closed head injury (CHI) and mild traumatic head injury are similar terms.

The terms are used somewhat interchangeably here. The preferred scientific term, mild traumatic brain injury (MTBI), will be used usually in this report.

The terminology as used here does not necessarily imply that every head injury is accompanied by brain damage. Some sequellae of head injuries are transient disruptions of brain function. Some symptoms are caused by injury to other head structures such as the inner ear, or head and neck muscles and ligaments.

2.2. Epidemiology

Minor head injuries are common health problems. A US Census Bureau 1991 National Health Interview Survey estimated the annual incidence as 618 injuries per 100,000 persons (Sosin et al., 1996). Nearly, half were caused either by motor vehicle accidents (28%) or by sports and physical activity injuries (20%).

Extrapolating from these figures, we see that more than one-third of the population is expected to suffer a MTBI at some time during their life.

The Center for Disease Control and Prevention (CDC) reported that each year 1.4 million Americans suffered a head injury that brought them to medical attention (Langlois et al., 2004). Among those, 79% (1.1 million) were seen at an emergency department and then released home. The most common causes of those traumatic head injuries were falls, which were seen most frequently among persons below age 5 and above age 74 years. The annual incidence for adults varied from 400 per 100,000 for young adults and the elderly, to 200 per 100,000 for adults ages 55–75.

2.3. Early symptoms

MTBI produces symptoms of varying types and degrees (Alexander, 1995). The most well known immediate symptom is a brief loss of consciousness lasting seconds to minutes. Some mild injuries cause no unconsciousness (Kelly and Rosenberg, 1997). Some patients experience just a brief period of feeling and appearing dazed. Others suffer from confusion and a post-traumatic amnesia that may last for minutes to hours. Many patients have no focal neurologic signs on examination and have negative neuroimaging studies. When tested, the Glasgow coma scale (GCS) is scored at 13–15.

Other immediate features of concussion include:

- Vacant stare.
- Delayed verbal or motor responses.
- Inability to focus attention.
- Disorientation.
- Slurred or incoherent speech.
- Gross observable incoordination.
- Emotionality out of proportion to the circumstances.
- Memory deficits.

Patients commonly exhibit the following in the first minutes to hours:

- Headache.
- Dizziness or vertigo.
- Lack of awareness of surroundings.
- Nausea and vomiting.

2.4. Early recovery symptoms

Post-concussion syndrome (PCS) is commonly experienced during the recovery from a MTBI. Common immediate symptoms are attention and memory deficits seen on tests of divided attention and working memory, which may last for weeks. Older patients may take longer to clear. Patients with demanding vocations or certain personalities may be aware of deficits longer (Alexander, 1995). Over the subsequent days or weeks, PCS patients often experience symptoms that include (Kelly and Rosenberg, 1997):

- Persistent low-grade headache.
- Light-headedness.
- Poor attention and concentration.
- Memory dysfunction.
- Easy fatigability.
- Irritability and low frustration tolerance.
- Intolerance of bright lights or difficulty focusing vision.
- Intolerance of loud noises, sometimes ringing in the ears.
- Anxiety and depressed mood.
- Sleep disturbance.

2.5. Longer term and chronic symptoms

2.5.1. Recovery over weeks to months

For most patients, symptoms resolve within weeks or a few months. The shorter the period of prominent symptoms, the better the chances of complete long term improvement (Levin et al., 1979). Cognitive and neurologic impairment is greater among patients who have had multiple head injuries over time (Gronwall and Wrightson, 1975). Depth and duration of unconsciousness and duration of post-traumatic amnesia have been proposed as the best guides for estimating head injury severity (Alexander, 1995), and those factors are generally favorable in mild head injury.

Three months after MTBI, some patients still experience symptoms such as headache, irritability, anxiety, dizziness, fatigue and impaired concentration. In one study (Ingebrigtsen et al., 1998), 62% reported at least one symptom and 40% reported three or more. The incidence of common symptoms 3 months after injury were 42%

headaches, 36% forgetfulness, 30% fatigue, 28% irritability, 26% dizziness, 25% decrease concentration, 23% impatience, and 20% disturbed sleep. There was no association between age, gender, cause, severity, duration of amnesia and overall symptoms.

By 6 months after a mild traumatic head injury, about one-third of patients still report at least one symptom (de Kruijk et al., 2002; Hofman et al., 2001), most often headache, dizziness or drowsiness. Complaints of headache, dizziness or nausea at the emergency room (ER) after mild head injury was associated with symptom severity at 6 months. The fewer the symptoms at the ER, the better the long-term outcome. Patients who had abnormal magnetic resonance imaging (MRI) at the time of injury often had some cerebral atrophy when retested 6 months later (Hofman et al., 2001), but these findings did not correspond to performance on cognitive testing. Imaging abnormalities also were reported using single photon emission computed tomography (SPECT), but again these lacked correspondence to cognitive signs or symptoms (Hofman et al., 2001; Kant et al., 1997).

2.5.2. *Persistent post-concussive syndrome*

After a year, 10–15% of MTBI patients still reported significant symptoms (Alexander, 1995). The other 85–90% of patients effectively had recovered, although some still had mild symptoms. The term *permanent symptomatic persistent post-concussive syndrome* (PPCS) refers to the patients who still have significant symptoms a year after injury. Those symptoms most often are dizziness, headache, light and sound sensitivity, as well as cognitive and emotional complaints. The cognitive problems most often found are inattention, poor memory and reduced executive function. The emotional symptoms most often reported are irritability, depression, nervousness, discouragement and anger.

PPCS patients studied by Ettlin et al. (1992) nearly always had concomitant chronic pain and depression. A premorbid psychiatric diagnosis was present in nearly 30% of PPCS patients. At follow-up after injury, nearly 70% had at least one psychiatric diagnosis, most often depression, anxiety, panic disorder, or phobias. The mild head injury may well cause stress after the accident, leading to depression, anxiety and social disruption soon thereafter. If the secondary stress of the injury (e.g., job loss, finances, and family strain) overwhelms symptomatic treatment of PCS, the PPCS begins to emerge. The earliest signs maybe the onset of depression and worsening of symptoms—particularly headache. The injured person may become overprotected, 'the disabled person'. There is no traditional reliable biologic measure for, or organic basis of, PPCS (Alexander, 1995; Ettlin et al., 1992).

2.6. *Sports injuries*

Sports are a common setting for head injuries, more notably in soccer (Tysvaer et al., 1989; Lindsay et al., 1980), American football (Saunders and Harbaugh, 1984), boxing (Jordan and Zimmerman, 1990; Mawdsley and Ferguson, 1963) and horseback riding (Forster et al., 1976). Half of a professional soccer team complained of protracted and persistent symptoms commonly attributed to PCS including headache, irritability, dizziness, lack of concentration and impaired memory (Tysvaer et al., 1989). This was attributed to the cumulative effect of repeatedly heading the ball.

Second head injuries increase the risk for neurological sequellae when the second impact occurs within a few days after the first. That second impact syndrome may lead to malignant edema and a markedly increased intracranial pressure from cerebral vascular congestion or loss of autoregulation (Giza and Hovda, 2001; Kelly and Rosenberg, 1997). An otherwise unsuspected cerebral contusion from head injury can have grave consequences if a second minimal head injury is sustained (Saunders and Harbaugh, 1984).

Boxers can develop dementia and impaired motor control after years in the sport (Mawdsley and Ferguson, 1963). Second injury syndrome may be an important part of this process in boxers. Some governments have established regulations for certain sports, such as boxing, to lessen the long-term risk and severity of neurological injury.

2.7. *Psychiatric components*

There is a major overlap between the symptoms of PPSC and depression. This makes it difficult to distinguish between these entities (Satz et al., 1999). Some investigators have wondered whether there are any cognitive symptoms attributable to mild head injury alone. Beyond depression, Gaetz (2004) also discusses other factors that complicate the assessment of mild head injury including chronic pain, anxiety, litigation, and stress.

Lishman (1988) believes that the PPCS starts as an organic problem, but its long-term persistence is psychologically driven. Jacobson (1995) holds a contrasting viewpoint. He believes that the chronic state is multifactorial throughout its course, involving both organic and psychosocial components. He cites the Belfast studies to support his view (Fenton et al., 1993; McClelland et al., 1994; Montgomery et al., 1991). According to the Jacobson model, cerebral dysfunction is the chief mechanism immediately after mild head injury followed by anxiety and depression. Thereafter, selective attention to PPCS and secondary gain are more important in maintaining symptoms. Effective treatments include education, antidepressant medication and cognitive restructuring.

If PPCS is more so due to disordered behavioral function rather than a biological injury, we may expect that EEG and QEEG are insensitive to detecting the disorder.

2.8. Pathology and the processes of injury

2.8.1. Injury and forces

The primary mechanism of traumatic brain injury involves biomechanical forces (Gennarelli, 1994, 1993). Extensive research with computer models and animal studies models identified three basic biomechanical forces as important causes of closed head injury. These are acceleration, deceleration and rotation. Moving the head violently forward-and-back or side-to-side result in the brain being accelerated and then, when subsequently stopped, decelerated. The anterior, middle and posterior fossa of the human skull presents ridges and other bony physical restrictions to the base of the brain, particularly the temporal poles, which may damage the base of the brain during severe trauma.

Acceleration–deceleration injury can produce contusions and lacerations at the base of the brain, and also can cause tissue deformation. Tissues deformation is most pronounced when the head is exposed to violent rotational forces that cause brain tissue stretching. This biomechanical distortion results in shear stress, eventually leading to massive cell death associated with severe head injury and neuronal dysfunction in MTBI.

2.8.2. Massive discharge

At the moment of head injury, neurons discharge resulting in an extensive release of neurotransmitters followed by neuronal suppression (Walker et al., 1944; Yoshino et al., 1991, 1992). This discharge, in addition to the cell membrane's biomechanical stress, produce a massive ionic flux dramatically changing the intra- and extra-cellular environment (Katayama et al., 1990). Among the many neurotransmitters released at the time of injury, the ones capturing the most scientific attention have been the excitatory amino acids—particularly glutamate (Faden et al., 1989; Katayama et al., 1990). The flood of glutamate opens the pathophysiologic pathway to secondary cell death associated with excitotoxicity and the impaired cognitive functions that frequently following severe traumatic brain injury.

2.8.3. Excitotoxicity

In the first few moments after injury, the released glutamate binds its receptors and causes increased intracellular calcium (Ca^{++}) and sodium (Na^{+}) (Fineman et al., 1993; Osteen et al., 2001, 2004). As Na^{+} enters the cell, the change in osmolality results in the cell taking up water. Affecting primarily the glial cells, this results in cytocellular edema and is the primary mechanism behind brain swelling after injury. Along with the increase in intracellular Ca^{++} and Na^{+}, glutamate activation results in the release of potassium (K^{+}) thereby depolarizing the cell membrane (resembling 'spreading depression') and activating Na^{+}/K^{+} (ATPase) pumps (Katayama et al., 1990; Strong et al., 2002). The activation of these pumps, in order to restore ionic homeostasis, increases the cellular demand for energy (ATP) (Bergsneider et al., 1997, 2000; DeSalles et al., 1986; Kawamata et al., 1992, 1995; Yoshino et al., 1991, 1992). Unfortunately, increasing the production of ATP is challenging for cells that survive the initial insult, especially since increased intracellular Ca^{++} disrupts ordinary mitochondrial respiration. This, along with the well described loss of the ability of the injured brain to increase cerebral blood flow to meet metabolic demands (Ginsberg et al., 1997), can place cells into a state of energy crisis (Andersen and Marmarou, 1992).

2.8.4. Combined effects as a process

These neurochemical and neurometabolic events unfold in various regions, some of which last from weeks to months following injury (for details, see Giza and Hovda, 2001). Consequently, traumatic brain injury should be viewed as 'a process, not an event' (Gennarelli and Graham, 1998). In MTBI, events generally lead to eventual cellular and tissue recovery, whereas in more severe injury the events often lead to regions of widespread cell death.

2.8.5. Diffuse axonal injury

In addition to a potential state of energy crisis, the above described injury-induced ionic cascade can induced the formation of oxygen free radicals thereby destroying cell membranes through a process of lipid peroxidation (Hall, 1993). Such a scenario can result in secondary cell death (necrosis or apoptosis). However, it has most recently been thought to be responsible for the development of diffuse axonal injury (DAI) typically seen following severe head injury.

In earlier studies, investigators thought that DAI following trauma was due to the shear stress forces imposed on the brain by the biomechanical insult discussed above. This concept gained popularity from experimental models in the 1940s and 1950s with Holbourn (1943) and Strich (1956, 1961) suggesting that rotational forces sheared axons and blood vessels by stretching them beyond their tolerances. This conclusion was supported by the examination of postmortem material from patients who had suffered severe head injury (Hume Adams et al., 1989). Some argued that histological evidence for DAI in the cerebellum, brainstem, corpus callosum and other white matter tracks represented damage from small hemorrhages from small penetrating vessels, but, contrary to that hypothesis, clear evidence of axonal bulb formations were present. These post-traumatic axon bulbs are consistent with specific damage to axons, and their formation is due primarily to accumulation of intracellular material transported via axoplasmic flow becoming impeded within the proximal damaged axon. With post-traumatic axonal swelling taking up to 12–18 h to develop, it was not surprising that microglia clusters along with long tract degeneration was evident in autopsy from head injured patients who had survived for longer periods of time.

The findings of DAI following human traumatic brain injury are now not in question, but the mechanism has been revisited. Shearing injuries can occur in the brain during the most severe trauma, but this alone cannot explain all forms of DAI. Axons can tolerate being stretched up to 65% above their original size without breaking (Smith et al., 1999). Along with the temporal parameters associated with the formation of axonal bulbs discussed above, this suggests a more protracted process. As described by Povlishock and his colleagues (Maxwell et al., 1997, 2003; Povlishock and Christman, 1995; Povlishock and Jenkins, 1995; Povlishock et al., 1983), the same ionic cascade associated with the cell soma following injury also occurs within the axon. The membrane stretching at the time of injury instigates the axonal ionic flux. This injury-induced stretching of axons, although insufficient to cause shearing, results in a marked increase in intracellular Ca^{++} contributing to neurofilament compaction and ultimate disconnection. Lesser degrees of injury-induced Ca^{++} flux cause temporary injury, whereas greater degrees result in permanent damage. Gennarelli (1996) proposed four stages or degrees of such injury, with progressively greater degrees of ionic imbalance, impaired axoplasmic flow, and eventually irreversible Ca^{++} influx. Upon closer examination of histological specimens, injury-induced axonal damage is most prevalent in regions where biomechanical strains associated with injury are the most prominent. Consequently, these regions of axonal damage are more patchy, variable, multi-focal, or localized than once thought—resulting in suggestions that the term diffusion axonal injury might be changed to traumatic axonal injury (Gaetz, 2004).

2.8.6. Hemorrhage and ischemia

In more severe degrees of trauma, cells also are exposed to ischemia and toxicity from extravasated blood from vascular injury. Focal contusions, when present, typically appear at gyral apices as punctuate hemorrhages or hemorrhagic streaks (Gaetz, 2004). They appear predominantly within the frontal and temporal poles as well as the orbital frontal, inferolateral temporal, and suprasylvian cortex (Gennarelli and Graham, 1998). Focal areas of ischemia can develop exposing regions of the injured brain to reductions in oxygen. Trauma can compromise the integrity of the blood–brain barrier, exposing cells to blood products contributing to the formation of free radicals and subsequent lipid peroxidation. Focal areas of transient blood–brain barrier breakdown may be responsible for PCS syndromes (Korn et al., 2005). Finally, traumatic brain injury results in the loss of vasoreactivity, which, if significant, can produce vasogenic edema contributing to the increase in intracranial pressure induced by cell swelling and the presence of mass lesions (e.g. subdural hemotoma).

2.8.7. Mild brain injury

All of the above described cell and tissue consequences of human traumatic brain injury can contribute to neurological deficits in more severe degrees of trauma. However, placing these mechanisms of cellular disruption and potential vulnerability in the context of MTBI is challenging. Even the most seemingly straightforward neurological finding, that of unconsciousness, is difficult to explain when it occurs following MTBI.

2.8.8. Unconsciousness

Shaw (2002) recently reviewed five hypotheses about why a patient loses consciousness from a concussion. These are the vascular, reticular, centripetal, pontine cholinergic, and the convulsive hypothesis. Each has its supportive evidence and proponents. Shaw supports the convulsive hypothesis, in which the massive neuronal discharge interrupts consciousness like an epileptic seizure.

2.9. Injury and the EEG

Overall, many mechanisms of injury have been described especially for major head injury. The particular role of some processes in mild head injury may be subtler, transient, or may not occur at all in many patients. Modern models of head injury pathophysiology suggest that the process of injury can unfold over hours or possibly days. Many of these processes are reversible and not accompanied by permanent structural damage, corresponding to symptom resolution over days or weeks. Immediate symptoms may be similar to a post-ictal state or due to a spreading depression. Early post-concussive symptoms may be due to cellular injury from disrupted axoplasmic flow, or transient cellular impairment from oxidative stress or disrupted cytoplasmic homeostasis. Models also show processes through which irreversible injury can take place. Locations of injury may be difficult to predict. Many factors could tip the balance between complete resolution and persistent residual impairment. The second injury syndrome seems to show that the healing brain is in a temporarily vulnerable state.

What lessons can carry over to the study of EEG and QEEG after concussion or mild head injury? Several can be seen. The injuries and its biological sequellae occur in the first hours or possibly days. There is no clear basis for biological deterioration months or years later. There is no reason to expect concussion or mild head injury to cause EEG deterioration months or years later. Healing occurs over days to months. EEG improvement also is expected over days to months. The sites of injury vary. Even the more severe of injuries are often patchy, multi-focal, and variable. There is no special pathognomonic location. The site for finding EEG abnormalities is expected to vary among patients. There is no special biological process that would likely produce pathognomonic kinds of EEG changes. The EEG changes in MTBI are likely to be similar to those seen in many other congenital or acquired brain disorders.

3. EEG in mild traumatic brain injury

Many decades of research and clinical experience with routine EEG carry with them important lessons for clinical interpretation of studies on patients after MTBI. These are needed not only for clinical interpretation of the routine EEG, but also for our QEEG discussion below. After all, QEEG is just measurements made on the EEG.

3.1. EEG immediately after mild traumatic brain injury

There are no published studies of human EEG during a blow to the head sufficient to cause a lapse of consciousness. To understand better the immediate pathophysiology of human minor head injury, one must rely on animal research reports about EEG during experimental head injury. Immediate EEG changes in animal models often included *initial epileptiform activity* described variously as a high amplitude shape wave (Walker et al., 1994), low amplitude high frequency discharges (Hayes et al., 1988; Meyer, 1970), epileptiform discharges (Dixon et al., 1987; Meyer and Denny-Brown, 1955; Marmarou et al., 1994), or generalized high voltage spiking (Nilsson et al., 1994). This is followed quickly in all the experimental models by a period of *suppressed cortical activity*, often appearing nearly isoelectric (Denny-Brown and Russell, 1941; Dixon et al., 1987; Dow et al., 1945; Foltz et al., 1953; Hayes et al., 1988; Meyer, 1970; Meyer and Denny-Brown, 1955; Marmarou et al., 1994; Nilsson et al., 1994; Walker et al., 1944; Ward and Clark, 1948; Williams and Denny-Brown, 1941). Generalized EEG suppression lasted for ten seconds to several minutes, typically for 1–2 min. Shaw also reported major cortical suppression in somatosensory evoked potential cortical peaks for several minutes after a blow to the head (Shaw, 2002). Following the EEG suppression is a period of generalized slowing, gradually improving to a normal baseline EEG over 10 min to 1 h.

Human acute EEG recordings after concussion have been conducted in boxers and industrial injuries (Dow et al., 1944; Kaplan and Browder, 1954; Larsson et al., 1954; Pampus and Grote, 1956). The Dow study in a shipyard recorded EEG as quickly as 10–15 min after closed head injuries. Many of Dow's subjects showed little or no noticeable alteration in their EEG. Others had diffuse slowing, seen especially in those recordings made the soonest after injury. The slowing resolved quickly, e.g. within an hour. In some patients with a well-documented concussion, the EEG was normal even at 15 min after the injury. Boxers showed a reduced EEG amplitude and increased irregular theta activity within 15–30 min of a fight, more so after being knocked out (Larsson et al., 1954; Pampus and Grote, 1956).

Overall, immediately following a MTBI, the preponderance of evidence favors an EEG evolution from epileptiform, to suppressed (perhaps post-ictal), to diffusely slow, and then to normal, all in a very short time frame after the injury.

3.2. EEG changes hours to months after mild traumatic brain injury

Even from the time of Williams (1941a) full report on EEG in head injury, investigators appreciated that the EEG is often normal even just a few hours after mild head injury. The most common EEG changes seen after mild head injury are attenuated posterior alpha (Jung, 1950) and focal irregular slow wave activity with a preponderance of theta waves in the temporal region (Courjon and Scherzer, 1972; Schneider and Hubach, 1962).

Within 24 h of a MTBI, an EEG often is normal or close to normal (Dow et al., 1944; Meyer-Mickeleit, 1953; Scherzer, 1965; Williams, 1941a). Any focal EEG abnormality tends to disappear within 6 months (Koufen and Dichgans, 1978) to a few years (Meyer-Mickeleit, 1953) in a vast majority of cases. Posterior focal slowing may evolve into slight alpha asymmetry before disappearing (Courjon and Scherzer, 1972; Jung, 1953; Meyer-Mickeleit, 1953). However, such a minor alpha asymmetry is of dubious diagnostic value because such a change frequently occurs among normal people (Radermecker, 1964).

Within several weeks or months of a mild head injury, serial EEGs often show gradually increases in alpha frequency, e.g. from 9.0 Hz eventually to 10.0 Hz. This is presumed to be a gradual return to the patient's original dominant alpha frequency (Jung, 1953; Koufen and Dichgans, 1978; Meyer-Mickeleit, 1953; Scherzer, 1965). Mild diffuse theta disappears (Fenton, 1996). The Koufen and Dichgans (1978) study provides a good survey of these and other EEG changes. In that study, 344 adults with head injury were tested from 3 days to 1 year after injury. Overall, 51% of these MTBI patients showed an initial EEG abnormality three days after injury. In 40% of their patients, slowing was detectable only retrospectively after repeated testing. For example, an initially 9 Hz alpha gradually increased to 10 Hz, the presumed pre-injury baseline. Yet, 9 Hz is well within the normal alpha frequency for the general population. They saw generalized slowing in 43% of initial EEGs and focal slowing in 32%. Thirty percent of focal changes were contralateral to the impact. The majority of EEG abnormalities resolved within 3 months, and about 90% resolved within 1 year.

Among 31 patients tested within 24 h of minor head injury, von Bierbrauer et al. (1992) found that 50% had EEG changes. They followed 23 of those patients over the next 2 months. Among those patients, 82% showed abnormalities within 24 h, 73% at 1 week, 50% at 3 weeks and 32% at 2 months. The alpha frequency was 9 Hz immediately after the injury and gradually increased by about 1 Hz over 2 months. By the end of 2 months, most EEG abnormalities were intermittent dysrhythmias.

A low voltage EEG with attenuated alpha originally was suspected of being a sign of trauma (Courjon and Scherzer, 1972). But when this observation was evaluated further, the higher incidence of low voltage EEGs in subjects

undergoing medical expert examinations was shown to be due to anxiety and a tense expectancy, also termed 'psychogenic suppression of the alpha rhythm' (Scherzer, 1966). Jung (1953) and Meyer-Mickeleit (1953) reported that an attenuated alpha, low voltage EEG record occurs no more often after head injury than in the normal healthy population. Vogel (1963) found that the low-voltage EEG is usually an inherited variant of electric cerebral activity. Drowsiness, pain and other factors also can lead to alpha-poor records. Courjon and Scherzer (1972) concluded that a low voltage, low alpha EEG could not be considered a sign of an organic post-concussion syndrome.

At 6 months after a MTBI, Torres and Shapiro (1961) saw epileptiform EEG abnormalities no more often than among persons who had sustained only a whiplash injury. Post-traumatic epileptiform EEG abnormalities increased over time, whereas non-epileptiform EEG abnormalities did not.

Overall, within hours or days of a head injury, an EEG shows subtle to mild slowing in a majority of patients—at least when judged against the patients' eventual follow-up baseline. Changes include decreased alpha frequency as well as generalized and focal slowing. Those changes often are subtle, even still within the range of normal findings in the general population. Some patients have a clinically normal initial EEG even as early as 15 min after a concussion. EEG abnormalities often resolve completely within months. At months or years after a mild head injury, a low voltage alpha EEG pattern is more a sign of anxiety rather than head injury.

3.3. Correspondence between EEG changes and clinical symptoms

In initial months after injury, abnormalities are seen more often in the EEG than in the clinical exam, especially among patients who had few or no symptoms (Kelly and Rosenberg, 1997; Rumpl, 2005). EEG abnormalities were more common than clinical signs. Relatively few (23%) abnormal EEGs were accompanied by abnormal neurologic exam signs. At the same time, most patients (86%) with abnormal neurologic exam signs had an abnormal EEG (Koufen and Dichgans, 1978). EEG abnormalities corresponded to prolonged post-traumatic amnesia (Koufen and Dichgans, 1978). Patients with amnesia lasting more than 8 h invariably had an abnormal EEG. Most patients without amnesia had a normal EEG. EEG abnormalities did not correspond to post-traumatic vertigo, dizziness or nystagmus (Scherzer, 1966).

Therefore, even in these initial months, EEG is more often shows an abnormality than does the physical examination. Many of these EEG abnormalities are subclinical, e.g. they are laboratory findings that are not accompanied by any detectable clinical problems.

As time goes on, the correspondence is poor between EEG and clinical signs and symptoms (Courjon and Scherzer, 1972; Jung, 1953; Meyer-Mickeleit, 1953; Mifka and Scherzer, 1962; Radermecker, 1964). Some clinical deficits persist despite a normal EEG. Some EEG abnormalities persist despite a normal clinical presentation (Courjon and Scherzer, 1972; Mifka and Scherzer, 1962). Torres and Shapiro (1961) noted in whiplash patients that, 'Correlation between severity of clinical symptoms and degree of EEG abnormality was poor in most cases, especially when either the electrical or the clinical abnormality was more than mild'.

Correspondence was poorer between EEG and neuroimaging tests. EEG did not correspond well to the presence or location of MRI, CT or SPECT abnormalities (Kant et al., 1997; Kelly and Rosenberg, 1997; Rumpl, 2005).

Boxers' EEGs and symptoms were studied by Pampus and Grote (1956) and by Haglund and Persson (1990). EEGs were more often abnormal among young professional boxers who fought more fights, although such a relationship was not seen among amateur boxers. EEGs also were abnormal more often after a career with frequent fights. There was no correlation between EEG changes and the number of bouts, lost fights, or boxing career length. Abnormal EEGs did not predict clinical impairment. EEG abnormalities showed no correspondence to neurological findings (Roberts, 1969).

Boxers repeatedly knocked out can develop a chronic progressive post-traumatic encephalopathy, sometimes referred to as the punch-drunk state (Martland, 1928). Critchley (1957) found more EEG abnormalities among these boxers compared to more successful boxers, but found no correlation between the degree of chronic encephalopathy and any specific EEG change. Similar findings were reported by Johnson (1969) and Mawdsley and Ferguson (1963). The EEG may help assess the severity of trauma shortly after a bout, but it is not helpful in assessing subsequent or chronic clinical symptoms. There was no clinical correlation between EEG abnormalities and psychometric tests (Johnson, 1969).

Soccer or track and field athletes had fewer EEG abnormalities than boxers. Professional soccer players' EEGs sometimes showed slight focal slow activity or a posterior dominant rhythm below 8 Hz (Tysvaer et al., 1989). There was no correlation between EEG changes and frequency of heading the ball.

All this has led some authors to consider that the EEG is of very little practical value in follow up after head injury (Claes, 1961; LeBlanc, 1999; Meyer-Mickeleit, 1953; Muller, 1955; Mueller, 1957; Radermecker, 1964). PCS symptoms can be neither proven nor denied by any kind of EEG (Caveness, 1966; Courjon, 1962; Kugler, 1966).

A normal EEG long after a head injury does not allow for any conclusion about the severity of the original trauma (Courjon and Scherzer, 1972). Normalization of the EEG cannot be considered evidence of lack of initial anatomical injury. Even severe head injury can have a normal EEG at a later date. Brain electrical activity often returns to normal

long after mild or severe head injury, even though patients may continue to complain of headache, dizziness, etc.

Conversely, an EEG abnormality is not apt for proving an organic basis for a patient's complaints. Kugler (1966) and Radermecker (1961) warned against any attempt to 'objectivate' post-traumatic symptoms by means of an EEG recording. Even substantial EEG abnormalities are not necessarily correlated with PCS symptoms (Courjon and Scherzer, 1972). Nor do EEG abnormalities predict the onset of PPCS (Ettlin et al., 1992).

Following EEG changes over time may be helpful (Courjon and Scherzer, 1972; Koufen and Dichgans, 1978). Post-traumatic EEG abnormalities tend to improve over months. If an EEG is unchanged throughout the entire posttraumatic period, it is probably not related to the trauma (Bickford and Klass, 1966 and Radermecker, 1964). Sometimes the EEG returns to normal even when neurologic or cognitive impairment persists, and in that case its normality is a sign of poor prognosis for subsequent clinical improvement (Lücking et al., 1977; Walter et al., 1948; Williams, 1941b; Strnad and Strnadová, 1987).

Low voltage alpha EEGs are seen in late post-traumatic syndrome and these seem largely to be due to anxiety (Scherzer, 1966). Many other normal situations, technical factors and other clinical conditions also can produce a low-amplitude alpha EEG. At any rate, a low voltage EEG should not be considered proof of the presence of an organic post-traumatic syndrome.

Overall, EEG abnormalities are more common than clinical symptoms in the initial months after a MTBI. Patients with an abnormal exam generally have an abnormal EEG, although many more EEG abnormalities are sub-clinical. Later after the injury, there is poor correspondence between EEG and clinical signs, symptoms, imaging results or psychometric tests. EEG abnormalities are seen with some sports injuries, but those findings do not usually correspond to clinical findings. Decreased posterior alpha long after injury is more likely due to anxiety rather than brain damage. EEG does not predict, confirm or measure PCS or PPCS, nor should mild EEG abnormality be used to substantiate an objective clinical brain injury. Nor can a normal EEG exclude an initial significant brain injury.

3.4. More serious head injuries

EEG findings in post-traumatic coma are beyond the scope of this review. Yet, the characteristics of EEG after severe injury have some bearing on the kinds of EEG changes expected after a MTBI. For that reason they are described here briefly.

EEG correlates well with the depth of post-traumatic coma (Arfel, 1972; Bricolo and Turella, 1973; Chatrian et al., 1963; Rumpl, 1979; Silverman, 1963; Stone et al., 1988; Synek, 1990). After a severe head injury, EEG findings range from increased slow activity to amplitude suppression with greater injuries (Rumpl, 1979, 2005). Post-traumatic coma also can show features more typical of sleep or various sharply contoured discharges, epileptic spikes, periodic lateralized epileptiform discharges (PLEDs), and triphasic waves. Reactivity and typical sleep features are more common among patients who make a good recovery (Rumpl et al., 1983).

Long after major closed or penetrating injuries, EEGs showed a wide variety of dysrhythmias, focal or generalized suppression, focal slowing, frontal alpha, and epileptiform discharges (Dawson et al., 1951; Jabbari et al., 1986; Ruijs et al., 1994; Lücking et al., 1977). Clinical improvement occurred faster than EEG improvement. Patients had more favorable outcomes when they more quickly progressed from slowing to normal alpha activity. Focal slowing or epileptiform discharges were seen more often among patients who had persistent clinical problems. The site of focal EEG features correlated poorly with the site of trauma. A severely abnormal EEG at the time of injury predicted more severe long-term neurologic sequellae, but mild to moderate EEG abnormalities did not help to predict clinical outcome. No prognostic or diagnostic significance could be deduced from factors such as generalized decreased amplitude.

ICU monitoring can add prognostic clues (Nuwer, 1994). Non-reactive and poorly variable EEGs predict a poorer outcome (Vespa et al., 2002). Such EEG changes accompanied by metabolic derangements predict particularly poor outcomes (Glenn et al., 2003; Vespa et al., 2003). Those metabolic markers show that the pathophysiology of moderate to severe head injury differs from that of MTBI.

Koufen et al. (1987) followed over 2 years a series of 100 patients who were delirious for more than 1 week after injury. EEG showed generalized slowing. By 3 months after the injury, the EEG was normal in half of the patients. Slowing rarely lasted longer than 6 months. Later, generalized abnormalities were seen in 70% of patients, and focal changes in 95%. Half of the patients with focal EEG abnormalities had focal neurological signs or symptoms. Generalized slowing took longer than focal to resolve, but disappeared more completely. Focal slowing persisted more than 2 years in 22%, mostly in those patients who had developed post-traumatic epilepsy.

Overall, several lessons carry over to the study of MTBI. A wide variety of abnormal EEG patterns are seen after severe trauma, none of which are pathognomonic of trauma per se. Mild EEG abnormalities did not predict neurologic outcome. EEGs gradually renormalized in many severe head injury patients, more quickly and completely for generalized slowing than for focal slowing.

3.5. Problems using EEG for diagnosis and prognosis after mild traumatic brain injury

The two prominent French and Austrian neurologists and neurophysiologists J. Courjon and E. Scherzer warned long ago about problematic or misleading use of EEG.

Table 1
On the use of EEG after mild traumatic head injury, Courjon and Scherzer (1972) noted

- EEG changes are not specific to a particular cause
- At a late stage after an injury, an EEG record is of little diagnostic or prognostic value
- Many different types of illness, injury or developmental problems can lead to the same EEG result
- Many normal processes can lead to EEG findings that can be mistaken for abnormality
- Normal EEG results do not ensure that a patient does not have brain injury from a mild head injury
- Abnormal EEG results do not ensure that a patient does have a brain injury from a mild head injury
- No conclusion can be drawn from the EEG as to the degree of working capacity, post-concussion syndrome, or neurological deficit
- Low amplitude alpha should not be considered indicative of head injury, but is commonly due to anxiety of other non-specific, non-diagnostic factors
- A non-expert often draws incorrect conclusions
- Fallaciously oversimplified EEG results are a disservice to legal proceedings

These concerns were published in the *Handbook of Electroencephalography and Clinical Neurophysiology* (Courjon and Scherzer, 1972). See Table 1 for a summary of their comments. These warnings apply especially to MTBI. Although originally penned for routine EEG, their comments apply well too to QEEG. They noted, 'The implications drawn from a detailed EEG report can never be absolute and imperative, apart from very rare exceptions. The electroencephalographer has to enumerate all the etiological possibilities of a certain EEG picture and give the degree of their probability in accordance with the clinical data'. Many laypersons and non-experts entertain 'mystical ideas about what exceptional insights into brain function an EEG investigation can provide'. These comments are as valid now as they were three decades ago.

Regarding misleading and oversimplified interpretations of EEG in medical–legal settings, Courjon and Scherzer warned, 'Either it is deduced from a pathological EEG that traumatic brain damage has occurred which may be the cause of subjective symptoms, or from a normal EEG it is deduced that no traumatic brain damage could have occurred and that no subjective symptoms should be present. Both conclusions are obviously fallacious'.

These issues and warnings about routine traditional EEG should be kept in mind when reviewing QEEG studies and claims.

4. QEEG in mild traumatic brain injury

Before discussing QEEG in MTBI, several background issues need to be reviewed. These include QEEG terminology and general problems encountered with QEEG testing for clinical disorders. In addition, there are general issues to be considered for how one assesses the clinical usefulness of a diagnostic test. With this background we best can discuss the clinical utility of QEEG for MTBI.

4.1. QEEG techniques and terminology

The following is a brief overview of QEEG terms, especially those used in the literature review further below. More extensive discussion of terms and techniques is found in Nuwer (1988).

Digital EEG is paperless recording, storage and display with many advantages over traditional paper recordings. *Quantitative EEG* (QEEG) is any mathematical or statistical analysis along with the various graphical displays made from digital EEG (Nuwer, 1988).

There are many varied QEEG techniques. *Automated event detection* uses mathematical algorithms to detect or identify interesting events such as possible epileptic spikes or non-convulsive seizures. Much false identification occurs, so human expert review is needed. *Monitoring and trending* of EEG uses mathematical algorithms to extract simple measurements from the EEG. Trending highlights EEG changes over hours or days in the intensive care unit or during surgery. That trending identifies changes that warn of possible complications. *Source analysis* tries to identify the brain location that generates certain brain waves. Scalp voltage distribution is compared to the distribution expected if the voltages were generated by a single dipole at specific intracranial site. This approximation is subject to failure in its assumptions that result in erroneous localization. All these techniques require expert human review at each stage of EEG processing to try to minimize error rates.

Frequency analysis converts the EEG into its frequency content, estimating how much energy occurred in each frequency band. This is expressed either in a few traditional EEG frequency bands, or as a continuous graph of frequency content from 0 to 30 Hz. It may be measured as power, or as the square root of power that usually is referred to as EEG amplitude.

Coherence analysis measures EEG at two separate sites, and scores how much that activity rises and falls synchronously. It usually is measured within each frequency band. Short distance coherence is made from adjacent scalp electrode sites (e.g. F3 and C3), as opposed to long distance coherence from recording sites farther apart.

EEG brain maps are graphical displays that typically illustrate the scalp distribution of EEG features. They can aid communication with non-specialists about the presence and location of certain EEG features. These stylized maps superficially resemble brain MRI or CT images, but that resemblance is purely superficial. EEG brain maps actually have relatively few real data points, so most of the image is just an extrapolation among those few real points. EEG brain maps often use color-coding to represent intensities of some feature e.g., scalp locations of EEG slow waves.

Normative statistical analysis compares a patient's EEG features to those from a group of normal subjects. Such comparisons may use frequency analysis or other EEG features. Typical measurements are expressed in terms of standard deviations away from a normal mean value, usually referred to as the *Z-score* for the feature. Statistical analysis can be displayed as numerical tables or as EEG brain maps of Z-scores. Numerical tables composed of hundreds or thousands of Z-scores are referred to here as *QEEG panels*.

Diagnostic discriminant analysis compares EEG features from a patient to those from a group of patients with a particular disorder. This tries to match a patient's EEG Z-scores to the pattern typical for a particular disorder. The results are expressed in terms of a diagnostic likelihood such as, 'This patient's findings are consistent with mild head injury with a probability of $P<0.05$'.

It is important to distinguish between panels and discriminants. The two have been confused repeatedly in published discussions. To further complicate the picture, both panels and discriminants come in a variety of different forms that must be evaluated separately. For example, consider Tests A and B that are run with different measurements and different calculations on different machines using different normative databases. Just because Test A can achieve a certain result does not prove that Test B can do the same. Instead, Test B needs its own evaluation and validation. To claim that Test B should be accepted, just because test A has been shown to work, is erroneous. Such an error occurs frequently in QEEG discussions.

Commercial vendors market specific combinations of QEEG techniques under commercial trade names such as *Neurometrics*. Typically these include QEEG panels of normative statistical frequency and coherence analysis. EEG brain maps and diagnostic discriminants often accompany Z-score tables. Commercial discriminants and QEEG panels are advertised to diagnose MTBI as well as alcoholism, substance abuse, dementia, depression, learning disorders, and many other medical problems.

4.2. Assessing QEEG as a diagnostic test

4.2.1. Assessing diagnostic tests

What is a diagnostic test? How do physicians determine a diagnostic test's acceptance for use?

A *diagnosis* is a professional opinion about the presence, absence, type, severity, or location of an illness, injury, or medical condition of a patient. A *differential diagnosis* is a group of diagnoses, among which is the likely cause of a patient's condition. A *diagnostic interpretation* is a diagnosis or differential diagnosis based on a test's findings. A *diagnostic test* is one on which such a diagnostic interpretation is based.

When used this way, QEEG is a diagnostic test and its interpretation is a diagnostic interpretation. That interpretation often will mention a diagnosis or differential diagnosis of disorders that could cause such test results. In most regions, making a diagnosis is part of the practice of medicine, and any person making diagnoses must do so within their licensed scope of practice for medicine or other limited-license health profession as regulated by their region's legal business and professions code. Sometimes QEEG is used instead as a research tool, which is beyond the scope of this review. Research tests are subject to their own regulations, institutional review boards, and informed consent forms.

Physicians use tests to narrow or prioritize a differential diagnosis. Test findings are useful when they are consistent with some possibilities but not with others, or strongly suggest some while only weakly supporting other diagnoses. If test results are consistent with one and only one diagnosis, the finding is considered *pathognomonic*. Medical tests rarely produce such a specific result.

Most neurological diagnoses are established through the history and physical examination. Diagnostic tests are used to confirm a diagnosis when there remains some doubt, or to narrow the differential diagnosis when the diagnosis remains unclear. Physicians have an armamentarium of available tests.

How do physicians decide when a new diagnostic test is valuable or effective in patient care? In practical terms, *medical usefulness* of a new diagnostic test is determined by the extent to which it can:

- Reduce the morbidity or mortality of a disease, by clarifying which medication, surgery, or other treatment is most likely to be effective, or by substituting a test with less risk for one with higher risks.
- Reduce the overall cost of the medical evaluation e.g., by replacing an inpatient procedure with an outpatient procedure.
- Substantially improve the patient's or family's understanding of the situation, leading to improved behavior or more accurate expectations.

Not all new information is clinically useful. Sometimes new information brings nothing of value to the care of the patient (Nuwer, 1990, 1992). Some is redundant, too nonspecific, too confusing, too risky, or too costly to obtain. This kind of problem is encountered in QEEG, where some proponents argue that any information is useful. That is an erroneous generalization that states, 'Some types of information are useful. This test provides information. Therefore, this information is useful'.

4.2.2. Assessing QEEG as a diagnostic test

Assessment of clinical usefulness includes several factors (Nuwer, 1992). The primary factor in the assessment is peer-reviewed published studies. Factors to consider in the literature review in general are presented in Table 2.

4.2.2.1. Cause and age of injury. The differential diagnosis for the cognitive complaints of post-concussion syndrome

Table 2
Factors to consider in evaluating QEEG literature

For review of diagnostic tests
- The published studies' quality
- What conclusions can be drawn from each study
- Whether those conclusions show medical usefulness
- The techniques' limitations and weaknesses
- The authors' conflicts of interest

Characteristics of quality studies
- The criteria for test 'abnormality' is defined clearly and prospectively
- Testing and interpretation is conducted blindly
- Patients and controls evaluated should be different from those used to create the test or database
- Patients should be representative of the diagnosis sought, e.g. mild traumatic brain injury
- Control patients should have other disorders from the same differential diagnosis
- Various assessments of validity should be measured, e.g. sensitivity, specificity
- Results should be compared to findings from history, physical exam, and other routine test results, e.g. EEG and neuro-imaging
- Studies should be conducted by impartial investigators independent from the companies or individuals with commercial interests

or mild head injury includes side effects of medication, depression and bipolar disorder, anxiety, panic attacks, post-traumatic stress disorder, insomnia and other sleep disorders, pre-existing mild brain disorders, early dementia, and other conditions. Drowsiness, anxiety and medications, including benzodiazepines and antidepressants, affect the EEG. If a QEEG shows 'abnormalities', what do those changes mean? How can those QEEG findings help to narrow the differential diagnosis?

How sensitive are mild head injury QEEG diagnostic discriminants to common injuries, such as striking a person's head on a cabinet door or slipping on an icy sidewalk? QEEG discriminants are marketed as sensitive to MTBI without an associated loss of consciousness and even injuries that are decades old. But, can they separate a recent injury from one long ago?

4.2.2.2. Value. One considers what clinical conclusions can be drawn. How does this help the patient? Simply providing information is not a demonstration that the information provided is useful. Sometimes this point has been difficult for non-clinicians to grasp. If a test brings little or no new information for narrowing the differential diagnosis, but does bring additional false-positive problems, potential for confusion, and added costs, then the new test will generally be judged to be medically not useful (Nuwer, 1998).

QEEG panels and discriminants often seem indiscriminant. QEEG panels provide hundreds or thousands of pieces of information e.g., measurements of many EEG features. Too often, no compelling rationale is presented for how the information is to be used to fulfill the clinical mission or effectiveness as discussed above. This is a major shortcoming of QEEG in MTBI patients.

4.2.3. Credibility threshold problems

Some factors make it more difficult to accept a study's conclusions. These are seen in many QEEG studies. One can speak of a threshold of credibility—the higher that threshold, the more difficult it is to get over that threshold and accept the study's conclusions. Several such factors are mentioned below. These should be considered as we assess the conclusions that can be drawn from QEEG studies.

Conflicts of interest, financial or otherwise, raise the possibility that the results have been contaminated during the research process. Many ways are possible for a researcher to affect a study's outcome. Such effects may be subtle, and do not necessarily imply any unethical or malicious behavior on the researcher's part. Nevertheless, a higher threshold needs to be achieved before accepting a study's results when the investigators are involved in commercialization and marketing of the study's product.

Notable past failures of QEEG's diagnostic capabilities raise concerns. QEEG has had problems. For example, one QEEG technique was reported and later marketed as an effective way to diagnose learning disabilities in school children (Ahn et al., 1980; Kaye et al., 1981). Yingling et al. (1986) disconfirmed this claim for children with dyslexia, the most common specific learning disability. Another report described a patient whose QEEG discriminant diagnosed schizophrenia as a cause for his complaints. Later, he turned out to have a brain tumor as the real cause (Nuwer and Hauser, 1994).

Black box techniques are ones for which the full methodological details are not published, often because they are considered proprietary business secrets. Complex black box techniques are difficult to verify. One must simply to accept them as they are. Some QEEG techniques are black box. That raises the threshold needed before accepting claims about them.

Spilt-half replication and jack-knife studies sometimes are claimed to be prospective studies. These studies collect their data before setting the normal limits used to interpret the results. This design leaves open the possibility that the collected data influence the normal limits that later were used to score the same data. These are more correctly categorized as retrospective trials because the methodology was not fully established until after the data was collected. A truly prospective study would have fully set forth detailed methods, normal limits, and process for determining results before collecting the data. Some QEEG studies use the split-half and jack-knife design. Those designs raise the threshold before accepting the studies' claims.

Confirmatory studies have much more credibility than exploratory studies. *Exploratory* studies make observations about interesting relationships in large data sets, but many of those detected relationships are just chance events. Confirmatory studies set forth specific hypotheses and methods in advance, and then test those hypotheses. Those hypotheses are falsifiable i.e., the hypothesis can be confirmed or not. Well-designed confirmatory studies have